

1. A transgenic, non-human mammal comprising erythrocytes that produce a human hemoglobin, but fail to produce adult hemoglobin endogenous to said non-human mammal.

5        2. The transgenic, non-human mammal of claim 1, wherein said erythrocytes fail to produce non-adult hemoglobin endogenous to said non-human mammal.

3. The transgenic, non-human mammal of claim 1, wherein said transgenic, non-human mammal is a mouse.

4. The transgenic, non-human mammal of claim 1, wherein said human hemoglobin is hemoglobin A.

5. The transgenic, non-human mammal of claim 1, wherein said human hemoglobin is sickle hemoglobin.

6. The transgenic, non-human mammal of claim 1, wherein said human hemoglobin is fetal hemoglobin.

7. The transgenic, non-human mammal of claim 1, wherein said human hemoglobin is an anti-sickling hemoglobin.

8. The transgenic, non-human mammal of claim 7, wherein said anti-sickling hemoglobin is selected from the group consisting of Hb AS1, Hb AS2, Hb AS3, Hb AS4, and Hb AS5.

9. The transgenic, non-human mammal of claim 1, wherein said human hemoglobin is hemoglobin Kansas Porto Alegre.

10. The transgenic, non-human mammal of claim 1, wherein said erythrocytes produce human fetal hemoglobin and human sickle hemoglobin.

11. The transgenic, non-human mammal of claim 1, wherein precursors of said erythrocytes each comprise a human hemoglobin gene comprising a thalassemic mutation.

12. The transgenic, non-human mammal of claim 11, wherein said precursors of said erythrocytes each further comprise a gene encoding a human  $\gamma$ -globin chain.

13. The transgenic, non-human mammal of claim 11, wherein said precursors of said erythrocytes each further comprise a gene encoding a human  $\beta$ -globin chain.

14. The transgenic, non-human mammal of claim 1, wherein said erythrocytes produce a human anti-sickling hemoglobin and human sickle hemoglobin.

15. The transgenic, non-human mammal of claim 1, wherein precursors of said erythrocytes each comprise a chromosome comprising a human  $\gamma$ -globin gene and a human  $\beta$ -globin gene.

16. The transgenic, non-human mammal of claim 1, wherein precursors of said erythrocytes each comprise a first chromosome comprising a human  $\gamma$ -globin gene and a

human  $\beta$ -globin gene, and a second chromosome comprising a human  $\epsilon$ -globin gene, a human  $\gamma$ -globin gene, a human  $\delta$ -globin gene, and a human  $\beta$ -globin gene.

17. The transgenic non-human mammal of claim 16, wherein said human  $\beta$ -globin gene encodes a  $\beta^s$  hemoglobin chain.

18. The transgenic, non-human mammal of claim 16, wherein precursors of said erythrocytes each comprise a first chromosome comprising a human  $\gamma$ -globin gene and a human  $\beta$ -globin gene, and a second chromosome comprising a human  $\epsilon$ -globin gene, two human  $\gamma$ -globin genes, a human  $\psi\beta$ -globin gene, a human  $\delta$ -globin gene, and a human  $\beta$ -globin gene.

19. A method of producing human hemoglobin, said method comprising expressing said human hemoglobin in the erythrocytes of a transgenic, non-human mammal of claim 1.

20. Human hemoglobin produced by the method of claim 19.

21. A method of testing a substance for efficacy in treating sickle cell anemia, said method comprising exposing a transgenic, non-human mammal of claim 5 to said substance and monitoring a characteristic of sickle cell anemia in said transgenic, non-human mammal following substance exposure, wherein amelioration of said characteristic of sickle cell anemia indicates a substance useful for treating sickle cell anemia.

22. The method of claim 21, wherein precursors of said erythrocytes each comprise a first chromosome comprising a human  $\gamma$ -globin gene and a human  $\beta$ -globin gene, and a second chromosome comprising a human  $\epsilon$ -globin gene, a human  $\gamma$ -globin gene, a human  $\delta$ -globin gene, and a human  $\beta^S$ -globin gene.

23. The method of claim 21, wherein said characteristic of sickle cell anemia is red blood cell sickling.

24. The method of claim 21, wherein said transgenic, non-human mammal is a mouse.